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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
MEHTA, ASHWIN D	

ART UNIT	PAPER NUMBER
1638	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/805,804	BAULCOMBE ET AL.	
	Examiner	Art Unit	
	Ashwin Mehta	1638	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 March 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *116-124* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *116-124* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 09/491,549.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *03112008*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. The amendments filed on March 3, 2008 were entered. The finality of the Office action mailed February 8, 2008 is removed.

2. The objection to the abstract under 35 U.S.C. 132(a) is withdrawn in light of its amendment.

3. The rejection of claims 116-124 under 35 U.S.C. 112, 1st paragraph is withdrawn in light of the claim amendments.

4. The rejection of claims 116-124 under 35 U.S.C. 102(e) is withdrawn in light of the claim amendments.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

5. Claims 116-124 are rejected under 35 U.S.C. 102(e) as being anticipated by Graham (U.S. Patent No. 6,573,099, issued June 3, 2003, filed June 19, 1998).

The claims are broadly drawn towards a method of silencing a gene in cells (the elected species is plants) by post-transcriptional gene silencing (PTGS), comprising introducing into cells short RNA molecules (SRMs) which are isolated short sense RNA molecules (SSRMs) and isolated short antisense RNA molecules (SARMs) at the same abundance, wherein the SARMs are complementary to any region of a target RNA transcribed from a gene which is silenced when said SRMs are present in cells containing said gene, and said SSRMs correspond to said target RNA, and wherein the nucleotide sequences of the SRMs consist of 20, 21, 22, 23, or 24 nucleotides, whereby said gene is silenced; or a method of silencing a gene in cells of a plant by PTGS, comprising introducing into said cells a composition of isolated SARMs and isolated SSRMs corresponding to a target RNA transcribed from said gene, the nucleotide sequences of which consist of 20, 21, 22, 23, or 24 nucleotides and wherein said SARMs can base pair with said target RNA, or wherein the SARMs and SSRMs are present at equal abundance; or said methods wherein the cells are contained in a plant and introducing comprises administering said SRMs to the plant, wherein the SRMs are synthetic, or wherein the gene is endogenous to the plant.

It is noted that in the Office action mailed June 26, 2007 on page 5, in reference to claim 116, the Examiner stated, "The term "isolated" in the recitations, "isolated short sense RNA molecules" and "isolated short antisense RNA molecules" indicates that SRMs are introduced into a plant cell by introduction of the short RNA molecules themselves into the cell, and not by introduction and transcription of a DNA construct encoding said SRMs." However upon

reconsideration, it is unclear that the introduction of SRMs should be limited in this manner. Further, the "composition" of the method of claim 120 is being interpreted to include vectors encoding the SARMs and SSRMs. Therefore, the methods of claims 116 and 120 are being broadly interpreted as also embracing the embodiment wherein the SARMs and SSRMs are being introduced into plant cells by transforming into plant cells vectors that encode the SARM and SSRM.

Graham teaches isolated genetic constructs, and vectors comprising them, comprising two copies of a structural gene sequence, wherein the structural gene sequence comprises a nucleotide sequence that is identical to a region of a target gene. The size of the structural gene sequences can be 20 to 30 nucleotides long, thus the nucleotide sequences may be 20, 21, 22, 23 or 24 nucleotides. One of the sequences is present in the sense orientation (and encode isolated short sense RNA molecules), the other in antisense (and encode isolated short antisense RNA molecules), both operably linked to the same or individual promoters. Graham teaches a method of introducing the constructs into cells of a plant, wherein the expressed RNA products encoded by the structural genes reduce the expression of the target gene (col. 1, lines 7-14; col. 4, lines 24-67; col. 6, lines 25-29; col. 7, lines 5-24; col. 13, lines 57-67). The expressed RNA product of the structural gene in antisense orientation inherently has the property of being capable of base pairing with the target RNA. The expressed RNA of the structural gene in sense orientation corresponds to the target RNA. When the same type of promoter is used to express the sense and antisense sequences, they would be present in equal abundance. The short RNAs encoded by the structural genes can be considered synthetic, as the synthetic genes are portions of genes and required recombinant DNA techniques for their production.

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. Claims 116-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fire et al. (U.S. Patent No. 6,506,559, issued January 14, 2003, filed December 18, 1998) in view of Graham (U.S. Patent No. 6,573,099, issued June 3, 2003, filed June 19, 1998).

The claims are broadly drawn towards a method of silencing a gene in cells (the elected species is plants) by post-transcriptional gene silencing (PTGS), comprising introducing into cells short RNA molecules (SRMs) which are isolated short sense RNA molecules (SSRMs) and isolated short antisense RNA molecules (SARMs) at the same abundance, wherein the SARMs are complementary to any region of a target RNA transcribed from a gene which is silenced when said SRMs are present in cells containing said gene, and said SSRMs correspond to said target RNA, and wherein the nucleotide sequences of the SRMs consist of 20, 21, 22, 23, or 24 nucleotides, whereby said gene is silenced; or a method of silencing a gene in cells of a plant by PTGS, comprising introducing into said cells a composition of isolated SARMs and isolated SSRMs corresponding to a target RNA transcribed from said gene, the nucleotide sequences of which consist of 20, 21, 22, 23, or 24 nucleotides and wherein said SARMs can base pair with said target RNA, or wherein the SARMs and SSRMs are present at equal abundance; or said

methods wherein the cells are contained in a plant and introducing comprises administering said SRMs to the plant, wherein the SRMs are synthetic, or wherein the gene is endogenous to the plant.

This rejection is addressing the embodiment encompassed by the claims wherein the RNA molecules themselves are introduced directly into plant cells.

Fire et al. teach a method of silencing a target gene post-transcriptionally in plant cells or plants, comprising introduction of a dsRNA wherein one of the strands is complementary to a portion of the target gene. The method comprises introducing into cells short RNA molecules that are complementary and are in sense and antisense orientation with respect to a portion of the target gene sequence. As the sense and antisense RNA molecules form a double strand, they are present in equal abundance. The target gene may be any gene, including endogenous genes. The RNA may be synthesized chemically, indicating that synthetic short RNA molecules are taught by the reference (col. 6, line 32-col. 8, line 6; col. 8, line 32-col. 9, line 25; col. 11, lines 8-55; claims). Claim 1 of Fire et al. does not recite any length for the RNA molecules. Claim 10 of Fire et al., which depends from claim 1, and further limits the scope of claim 1, limits the size of the RNA sequences to be at least 25 bases. Therefore, parent claim 1 encompasses RNA sequences that are also shorter than 25 bases in length.

Fire et al. do not actually disclose RNA molecules that are 20, 21, 22, 23, or 24 nucleotides.

Graham et al. teach a method of expressing in plant cells sense sequences corresponding to a target gene, and antisense sequences complementary to said target gene, to repress

expression of said gene, wherein the sense and antisense sequences can be 20-30 nucleotides long, as discussed above.

It would have been obvious and within the scope of one of ordinary skill in the art to use the method of Fire et al. to introduce into plants double-stranded RNA molecules to inhibit expression of a target gene, by making the RNA molecules 20-24 nucleotides long. Graham teaches that expressed RNA sequences that repress a target gene of interest can be 20-30 nucleotides long. It therefore would have been obvious to the double-stranded RNA of Fire et al. 20, 21, 22, 23, or 24 nucleotides long, as they are all within 20-30 nucleotides in length and are considered functional equivalents. The nucleic acid fragments were obviously synthetic, as their construction required recombinant DNA techniques.

7. Claims 116-124 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brown et al. (U.S. Patent No. 6,723,987, issued April 20, 2004, filed August 19, 1999).

The claims are broadly drawn towards a method of silencing a gene in cells (the elected species is plants) by post-transcriptional gene silencing (PTGS), comprising introducing into cells short RNA molecules (SRMs) which are isolated short sense RNA molecules (SSRMs) and isolated short antisense RNA molecules (SARMs) at the same abundance, wherein the SARMs are complementary to any region of a target RNA transcribed from a gene which is silenced when said SRMs are present in cells containing said gene, and said SSRMs correspond to said target RNA, and wherein the nucleotide sequences of the SRMs consist of 20, 21, 22, 23, or 24 nucleotides, whereby said gene is silenced; or a method of silencing a gene in cells of a plant by PTGS, comprising introducing into said cells a composition of isolated SARMs and isolated

SSRMs corresponding to a target RNA transcribed from said gene, the nucleotide sequences of which consist of 20, 21, 22, 23, or 24 nucleotides and wherein said SARMs can base pair with said target RNA, or wherein the SARMs and SSRMs are present at equal abundance; or said methods wherein the cells are contained in a plant and introducing comprises administering said SRMs to the plant, wherein the SRMs are synthetic, or wherein the gene is endogenous to the plant.

Brown et al. teach methods to inhibit the expression of an endogenous gene encoding an enzyme of the gibberellin (GA) synthesis pathway in plants. The method comprises expressing a coding sequence, or fragment thereof, of an enzyme of the GA synthesis pathway in the plant in antisense orientation or in sense orientation to cause co-suppression. Fragment sizes include those that are at least 20 or 24 nucleotides long. The nucleic acid fragment could be introduced into the plants from DNA or RNA expression vectors (col. 3, lines 49-67: col. 16, line 66 to col. 20, line 27; col. 21, lines 57-63).

Brown et al. do not disclose using anti-sense and co-suppression strategies simultaneously to inhibit the expression of a target gene.

It would have been obvious and within the scope of one of ordinary skill in the art to modify the method of Brown et al. by expressing a fragment of a coding sequence of the GA synthesis pathway in the sense and antisense orientation at the same time. Note that the fragments need not target the same region of target gene. It would have been obvious to make the fragment sizes to be 20-24 nucleotides long, as this is within the size range taught by Brown et al. All such fragment sizes are considered functional equivalents. The nucleic acid fragments were obviously synthetic, as their construction required recombinant DNA techniques. One

would have been motivated to inhibit target gene expression by using antisense and co-suppression strategies at the same time, as the use of two strategies to inhibit gene expression would have given a greater likelihood of success.

Contact Information

Any inquiry concerning this or earlier communications from the Examiner should be directed to Ashwin Mehta, whose telephone number is 571-272-0803. The Examiner can normally be reached from 8:00 A.M to 5:30 P.M. If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Anne Marie Grunberg, can be reached at 571-272-0975. The fax phone numbers for the organization where this application or proceeding is assigned are 571-273-8300. Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov.

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April 11, 2008

/Ashwin Mehta/
Primary Examiner, Art Unit 1638